Jessie De Graef
Ghent University

Glutamate-gated chloride genes in ivermectin-resistant *Cooperia oncophora*

De Graef J.[1], Claerebout E.[1], Vercruysse J.[1], Wolstenholme A.[2], Mitreva M.[3], Geldhof P.[1]
[1]Laboratory for Parasitology, Faculty of Veterinary Medicine, Ghent University, Belgium.
[2]Department of Infectious Diseases, University of Georgia, Athens, Georgia, United States of America.
[3]Department of Genetics, The Genome Center, Washington University School of Medicine, St. Louis, Missouri, United States of America.

The glutamate-gated chloride-channels (GluCl's) are only found in invertebrates and are important target sites for macrocyclic lactones (ML's). Changes at the protein level of the ML-target sites may induce resistance to the anthelmintics. In the free living nematode *Caenorhabditis elegans,* six genes have been identified that encode GluCl subunits. In this study we analysed the transcriptome database of *C. oncophora* for genes that encode possible GluCl subunits. We could identify homologues of *Avr-14*, *Glc-2*, *Glc-4* and a parasite-specific GluCl gene, i.e. *Glc-6*. By reverse-transcriptase PCR we determined that all these genes are equally expressed in all life stages (L1, L2, L3, L4, Male, Female) of *C. oncophora*, except for a lower transcription in the eggs. Full-length cDNA sequences of *Glc-4* and *Glc-6* were generated from a susceptible and ivermectin-resistant isolate and subsequently analyzed for the presence of polymorphisms. In addition, quantitative real-time PCR's were performed to compare the mRNA transcription levels between susceptible and resistant *C. oncophora* adult worms. For *Glc-4* no constitutive or inducible changes could be observed. In contrast, we found a significant downregulation of *Glc-6* transcription levels in resistant adult worms compared to susceptible ones, similar as previously described for *Avr-14*. The search for relevant mutations, indicating ivermectin-resistance in these *GluCl* genes is currently ongoing.